

CLAIMS

1. A peptide which mimics a loop on the γ -chain that either interact with a cytokine or a γ -chain partner receptor chain of a heterodimeric cytokine receptor, wherein said peptide consists of 5-25 amino acids and inhibits signal transduction mediated by cytokine:receptor binding of cytokines that bind to receptors that comprise a γ -chain.
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2. The peptide of claim 1 wherein said peptide includes: SEQ ID NO:1 IQLYQTF; SEQ ID NO:2 IHLYQTF; SEQ ID NO:3 CLQYLV; SEQ ID NO:4 CLEHLV; SEQ ID NO:5 CLQYLT; SEQ ID NO:6 CLEHLT; SEQ ID NO:7 CLQYLTQ; SEQ ID NO:8 CLEHLTQ; SEQ ID NO:9 PIAGSSQQ; SEQ ID NO:10 PLCGSAQH; SEQ ID NO:11 PLAGSAQH; SEQ ID NO:12 NHEPRFLS; SEQ ID NO:13 DYRHKFSL; SEQ ID NO:14 LNLQNL; SEQ ID NO:15 LKLQNL; SEQ ID NO:16 NLSESQL; SEQ ID NO:17 KLSEQL or such an amino acid sequence with one or more conservative substitutions.
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3. The peptide of claim 1 wherein said peptide includes: SEQ ID NO:1 IQLYQTF; SEQ ID NO: 2 IHLYQTF; SEQ ID NO:3 CLQYLV; SEQ ID NO:4 CLEHLV; SEQ ID NO:5 CLQYLT; SEQ ID NO:6 CLEHLT; SEQ ID NO:7 CLQYLTQ; SEQ ID NO:8 CLEHLTQ; SEQ ID NO:9 PIAGSSQQ; SEQ ID NO:10 PLCGSAQH; SEQ ID NO:11 PLAGSAQH; SEQ ID NO:12 NHEPRFLS; SEQ ID NO:13 DYRHKFSL; SEQ ID NO:14 LNLQNL; SEQ ID NO:15 LKLQNL; SEQ ID NO:16 NLSESQL or SEQ ID NO:17 KLSEQL.
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4. The peptide of claim 1 wherein said peptide includes: SEQ ID NO:1 IQLYQTF; SEQ ID NO: 2 IHLYQTF; SEQ ID NO:3 CLQYLV; SEQ ID NO:4 CLEHLV; SEQ ID NO:5 CLQYLT; SEQ ID NO:6 CLEHLT; SEQ ID NO:7 CLQYLTQ; SEQ ID NO:8 CLEHLTQ; SEQ ID NO:9 PIAGSSQQ; SEQ ID NO:10 PLCGSAQH; SEQ ID NO:11 PLAGSAQH; SEQ ID NO:12 NHEPRFLS; SEQ ID NO:13 DYRHKFSL; SEQ ID NO:14 LNLQNL; SEQ ID NO:15 LKLQNL; SEQ ID NO:16 NLSESQL; SEQ ID NO:17 KLSEQL or such an amino acid sequence with one or more conservative substitutions.
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5. The peptide of claim 1 wherein said peptide is conformationally restricted.

6. The peptide of claim 1 wherein said peptide is cyclic.

7. The peptide of claim 1 wherein said peptide has a 5 cysteine residue at its N terminus and a cysteine residue at its C terminus and it is cyclized by formation of a disulfide bond between said cysteine residues.

8. The peptide of claim 1 wherein said peptide is selected from the group consisting of: SEQ ID NO:18 CIQLYQTFC; 10 SEQ ID NO:19 CIHLYQTFC; SEQ ID NO:20 CLQYLVC; SEQ ID NO:21 CLEHLVC; SEQ ID NO:22 CLQYLTC; SEQ ID NO:23 CLEHLTC; SEQ ID NO:24 CLQYLTQC; SEQ ID NO:25 CLEHLTQC; SEQ ID NO:26 CPIAGSSQQC; SEQ ID NO:37 CPICGSSQQC; SEQ ID NO:27 CPLCGSAQHC; SEQ ID NO:28 CPLAGSAQHC; SEQ ID NO:29 CNHEPRFLSC; SEQ ID NO:30 CDYRHKFSLC; 15 SEQ ID NO:31 CLNLQNL; SEQ ID NO:32 CLKLNQNL; SEQ ID NO:33 CNLSESQLC; SEQ ID NO:34 CKLSESQLC and derivative peptides thereof.

9. The peptide of claim 1 wherein said peptide is selected from the group consisting of: SEQ ID NO:18 CIQLYQTFC; 20 SEQ ID NO:19 CIHLYQTFC; SEQ ID NO:20 CLQYLVC; SEQ ID NO:21 CLEHLVC; SEQ ID NO:22 CLQYLTC; SEQ ID NO:23 CLEHLTC; SEQ ID NO:24 CLQYLTQC; SEQ ID NO:25 CLEHLTQC; SEQ ID NO:26 CPIAGSSQQC; SEQ ID NO:37 CPICGSSQQC; SEQ ID NO:27 CPLCGSAQHC; SEQ ID NO:28 CPLAGSAQHC; SEQ ID NO:29 CNHEPRFLSC; SEQ ID NO:30 CDYRHKFSLC; 25 SEQ ID NO:31 CLNLQNL; SEQ ID NO:32 CLKLNQNL; SEQ ID NO:33 CNLSESQLC and SEQ ID NO:34 CKLSESQLC.

10. The peptide of claim 1 wherein said peptide is a conformationally restricted peptide having the formula:

$R_1 - R_2 - R_3 - R_4 - R_5$

30 wherein:

R_1 is a linking moiety;

R_2 is 0-10 amino acids;

R₃ is SEQ ID NO:1 IQLYQTF; SEQ ID NO: 2 IHLYQTF; SEQ ID NO:3 CLQYLV; SEQ ID NO:4 CLEHLV; SEQ ID NO:5 CLQYLT; SEQ ID NO:6 CLEHLT; SEQ ID NO:7 CLQYLTQ; SEQ ID NO:8 CLEHLTQ; SEQ ID NO:9 PIAGSSQQ; SEQ ID NO:36 PICGSSQQ; SEQ ID NO:10 PLCGSAQH; 5 SEQ ID NO:11 PLAGSAQH; SEQ ID NO:12 NHEPRFLS; SEQ ID NO:13 DYRHKFSL; SEQ ID NO:14 LNLQNL; SEQ ID NO:15 LKLQNL; SEQ ID NO:16 NLSESQL; SEQ ID NO:17 KLSEQL or such an amino acid sequence with one or more conservative substitutions;

10 R₄ is 0-10 amino acids; and
R₅ is a linking moiety.

11. The peptide of claim 10 wherein:

R₁ is cysteine; and
R₅ is cysteine.

12. The peptide of claim 11 wherein:

15 R₃ is SEQ ID NO:1 IQLYQTF; SEQ ID NO: 2 IHLYQTF; SEQ ID NO:3 CLQYLV; SEQ ID NO:4 CLEHLV; SEQ ID NO:5 CLQYLT; SEQ ID NO:6 CLEHLT; SEQ ID NO:7 CLQYLTQ; SEQ ID NO:8 CLEHLTQ; SEQ ID NO:9 PIAGSSQQ; SEQ ID NO:36 PICGSSQQ; SEQ ID NO:10 PLCGSAQH; SEQ ID NO:11 PLAGSAQH; SEQ ID NO:12 NHEPRFLS; SEQ ID NO:13 20 DYRHKFSL; SEQ ID NO:14 LNLQNL; SEQ ID NO:15 LKLQNL; SEQ ID NO:16 NLSESQL; or SEQ ID NO:17 KLSEQL.

13. The peptide of claim 12 wherein:

R₁ is cysteine; and
R₅ is cysteine.

25 14. A pharmaceutical composition comprising a peptide of claim 1 and a pharmaceutically acceptable carrier or diluent.

15. The pharmaceutical composition of claim 14 wherein said peptide includes: SEQ ID NO:1 IQLYQTF; SEQ ID NO: 2 IHLYQTF; SEQ ID NO:3 CLQYLV; SEQ ID NO:4 CLEHLV; SEQ ID NO:5 30 CLQYLT; SEQ ID NO:6 CLEHLT; SEQ ID NO:7 CLQYLTQ; SEQ ID NO:8 CLEHLTQ; SEQ ID NO:9 PIAGSSQQ; SEQ ID NO:10 PLCGSAQH; SEQ ID NO:11 PLAGSAQH; SEQ ID NO:12 NHEPRFLS; SEQ ID NO:13 DYRHKFSL;

SEQ ID NO:14 LNLQNL; SEQ ID NO:15 LKLQNL; SEQ ID NO:16 NLSESQL;
SEQ ID NO:17 KLSEQL or such an amino acid sequence with one or
more conservative substitutions.

16. The pharmaceutical composition of claim 14 wherein
5 said peptide includes: SEQ ID NO:1 IQLYQTF; SEQ ID NO: 2
IHLYQTF; SEQ ID NO:3 CLQYLV; SEQ ID NO:4 CLEHLV; SEQ ID NO:5
CLQYLT; SEQ ID NO:6 CLEHLT; SEQ ID NO:7 CLQYLTQ; SEQ ID NO:8
CLEHLTQ; SEQ ID NO:9 PIAGSSQQ; SEQ ID NO:36 PICGSSQQ; SEQ ID
NO:10 PLCGSAQH; SEQ ID NO:11 PLAGSAQH; SEQ ID NO:12 NHEPRFLS;
10 SEQ ID NO:13 DYRHKFSL; SEQ ID NO:14 LNLQNL; SEQ ID NO:15
LKLQNL; SEQ ID NO:16 NLSESQL or SEQ ID NO:17 KLSEQL.

17. The pharmaceutical composition of claim 14 wherein
said peptide is conformationally restricted.

18. The pharmaceutical composition of claim 14 wherein
15 said peptide is cyclic.

19. The pharmaceutical composition of claim 14 wherein
said peptide has a cysteine residue at its N terminus and a
cysteine residue at its C terminus and it is cyclized by
formation of a disulfide bond between said cysteine residues.

20 20. The pharmaceutical composition of claim 14 wherein
said peptide is selected from the group consisting of: SEQ ID
NO:18 CIQLYQTFC; SEQ ID NO:19 CIHLYQTFC; SEQ ID NO:20 CLQYLVC;
SEQ ID NO:21 CLEHLVC; SEQ ID NO:22 CLQYLTC; SEQ ID NO:23
CLEHLTC; SEQ ID NO:24 CLQYLTQC; SEQ ID NO:25 CLEHLTQC; SEQ ID
25 NO:26 CPIAGSSQQC; SEQ ID NO:37 CPICGSSQQC; SEQ ID NO:27
CPLCGSAQHC; SEQ ID NO:28 CPLAGSAQHC; SEQ ID NO:29 CNHEPRFLSC;
SEQ ID NO:30 CDYRHKFSLC; SEQ ID NO:31 CLNLQNL; SEQ ID NO:32
CLKLQNL; SEQ ID NO:33 CNLSESQLC; SEQ ID NO:34 CKLSESQLC and
derivative peptides thereof.

30 21. The pharmaceutical composition of claim 14 wherein
said peptide is selected from the group consisting of: SEQ ID

NO:18 CIQLYQTFC; SEQ ID NO:19 CIHLYQTFC; SEQ ID NO:20 CLQYLVC;
SEQ ID NO:21 CLEHLVC; SEQ ID NO:22 CLQYLTC; SEQ ID NO:23
CLEHLTC; SEQ ID NO:24 CLQYLTQC; SEQ ID NO:25 CLEHLTQC; SEQ ID
NO:26 CPIAGSSQQC; SEQ ID NO:37 CPICGSSQQC; SEQ ID NO:27
5 CPLCGSAQHC; SEQ ID NO:28 CPLAGSAQHC; SEQ ID NO:29 CNHEPRFLSC;
SEQ ID NO:30 CDYRHKFSLC; SEQ ID NO:31 CLNLQNL; SEQ ID NO:32
CLKLQNL; SEQ ID NO:33 CNLSESQLC and SEQ ID NO:34 CKLSESQLC.

22. The pharmaceutical composition of claim 14 wherein
said peptide is a conformationally restricted peptide having
10 the formula:

$$R_1 - R_2 - R_3 - R_4 - R_5$$

wherein:

R_1 is a linking moiety;

R_2 is 0-10 amino acids;

15 R_3 is SEQ ID NO:1 IQLYQTF; SEQ ID NO: 2 IHLYQTF; SEQ
ID NO:3 CLQYLV; SEQ ID NO:4 CLEHLV; SEQ ID NO:5 CLQYLT; SEQ ID
NO:6 CLEHLT; SEQ ID NO:7 CLQYLTQ; SEQ ID NO:8 CLEHLTQ; SEQ ID
NO:9 PIAGSSQQ; SEQ ID NO:36 PICGSSQQ; SEQ ID NO:10 PLCGSAQH;
SEQ ID NO:11 PLAGSAQH; SEQ ID NO:12 NHEPRFLS; SEQ ID NO:13
20 DYRHKFSL; SEQ ID NO:14 LNLQNL; SEQ ID NO:15 LKLQNL; SEQ ID
NO:16 NLSESQL; SEQ ID NO:17 KLSEQL or such an amino acid
sequence with one or more conservative substitutions;

R_4 is 0-10 amino acids; and

R_5 is a linking moiety.

25 23. The pharmaceutical composition of claim 14 wherein:
 R_1 is cysteine; and
 R_5 is cysteine.

24. The pharmaceutical composition of claim 23 wherein:

30 R_3 is SEQ ID NO:1 IQLYQTF; SEQ ID NO: 2 IHLYQTF; SEQ
ID NO:3 CLQYLV; SEQ ID NO:4 CLEHLV; SEQ ID NO:5 CLQYLT; SEQ ID
NO:6 CLEHLT; SEQ ID NO:7 CLQYLTQ; SEQ ID NO:8 CLEHLTQ; SEQ ID
NO:9 PIAGSSQQ; SEQ ID NO:36 PICGSSQQ; SEQ ID NO:10 PLCGSAQH;
SEQ ID NO:11 PLAGSAQH; SEQ ID NO:12 NHEPRFLS; SEQ ID NO:13

DYRHKFSL; SEQ ID NO:14 LNLQNL; SEQ ID NO:15 LKLQNL; SEQ ID NO:16 NLSESQL; or SEQ ID NO:17 KLSEQL.

25. The pharmaceutical composition of claim 24 wherein:

R₁ is cysteine; and

5 R₅ is cysteine.

26. A method of inhibiting signal transduction mediated by cytokine:receptor binding of cytokines that bind to receptors that comprise a γ -chain, said method comprising the step of administering an effective amount of a peptide of claim

10 1.

27. A method of inhibiting cytokine mediated cell growth, proliferation, function or activity comprising the step of contacting said cell with an peptide of claim 1.

28. A method of treating a patient suffering from a 15 disease disorder or condition characterized by cytokine mediated cell growth, proliferation, function or activity comprising the step of administering to said patient a therapeutically effective amount of a peptide of claim 1.

29. A method of treating a patient suffering from a 20 disease disorder or condition characterized by cytokine mediated cell growth, proliferation, function or activity comprising the step of administering to said patient a therapeutically effective amount of a peptide of claim 1, wherein said patient has lymphoma, leukemia, an allergic 25 reaction, an autoimmune disease, graft versus host disease or rejection of a transplant or graft.

30. A method of preventing a condition characterized by cytokine mediated cell growth, proliferation, function or activity in a patient identified as being at risk of such a 30 condition comprising the step of administering to said patient a prophylactically effective amount of a peptide of claim 1.

31. A method of preventing a condition characterized by cytokine mediated cell growth, proliferation, function or activity in a patient identified as being at risk of such a condition comprising the step of administering to said patient
5 a prophylactically effective amount of a peptide of claim 1, wherein said patient is at risk of an allergic reaction, graft versus host disease or rejection of a transplant or graft.